

Appl. Serial No. 10/826,094
Amendment dated January 27, 2005
Amendment filed with RCE

Confirmation No. 9255

REMARKS

Applicant respectfully requests entry of the Amendment and reconsideration of the claims. Rejected claims 1-3, 7-8, and 10-11 have been amended. No new matter has been added and support can be found throughout the specification, including at paragraph 20 of the instant specification. Please cancel claims 4, 9, 13-14, 17, 21-23, and 34-35 without prejudice. Applicant retains the right to pursue these claims through divisional and/or continuation applications.

Claims 16, 18-20, and 24-33 remain withdrawn. Withdrawn claims 18, 20, 24-27, and 30-31 are currently amended and withdrawn. As the Examiner is aware, where Applicant elects claims directed to a product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with MPEP § 821.04. Process claims that depend from or otherwise include all of the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 C.F.R. § 1.116.

In the advisory action dated December 7, 2005, the Examiner contends that the specification does not provide adequate support for the term "N-substituted maleimide". Applicant respectfully disagrees. Based on the number of species recited in the specification at paragraphs 20 and 75, the specification supports the claim of the genus of N-substituted maleimides. Additionally, the recited species were well known to be N-substituted maleimides as evidenced by the art cited by the Applicant (e.g., Zentz) and by the Examiner (Filho et al.). "Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces". *In re Wallach*, 378 F.3d 1330, 1334 (Fed. Cir. 2004). Applicant respectfully asserts that the specification provides sufficient disclosure to support the term "N-substituted maleimides."

Each of the recited species are representative examples of N-substituted maleimides. The fact that these species are N-substituted maleimides is a property that flows inherently from their structure and nomenclature, which is disclosed in the description. An applicant is allowed to rely on properties that flow inherently from the claimed subject matter (see, for example, *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1988).

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As such, Applicant respectfully asserts that the specification sufficiently supports the term "N-substituted maleimides".

Rejections under 35 U.S.C. § 103(a)

In the office action dated September 28, 2005, the Examiner rejected the claims under 35 U.S.C. § 103(a) for alleged obviousness. Specifically, the Examiner rejected a) claims 1-3, 5-8, and 10-12 over U.S. Pat. No. 5,688,516 (Raad et al.) in view of Filho et al. (cited in the IDS filed August 27, 2004); b) claims 1, 5-10, and 35 over U.S. Pat. No. 4,845,256 (Mcbes et al.) in view of Filho et al.; c) claims 1-2, 4-9, and 13-14 over U.S. Pat. Pub. No. 2002/0133169 (Berry) over Filho et al.; and d) claims 1-15 over U.S. Pat. No. 5,688,516 (Raad et al.) in view of Filho et al. and further in view of U.S. Pat. No. 6,528,107 (Chinn et al.). Applicant respectfully traverses.

Prima Facie Obviousness. To establish a *prima facie* case of obviousness, three criteria must be met--a suggestion or motivation to combine references, a reasonable expectation of success, and the prior art reference teaches or suggests all the claim limitations. MPEP §2143; *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Applicant respectfully asserts that there is no reasonable expectation of success nor do the prior art references teach or suggest all of the claim limitations. Applicant respectfully asserts that the Examiner has not met the criteria for establishing obviousness under 35 U.S.C. §103(a).

Unexpected Success. Evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. MPEP 716.02; *In re Chapp*, 816 F.2d 643, 646 (Fed. Cir. 1987).

A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness...of the claims at issue. *In re Corkill*, 771 F.2d 1496, 1501 (Fed. Cir. 1995); MPEP 716.02(a).

Evidence of a greater than expected result may be shown by demonstrating an effect that is greater than the sum of each of the separate effects. *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 809 (Fed. Cir. 1989); MPEP 716.02(a).

A. ***Raad et al. in view of Filho et al.*** Applicant maintains that original claim 1 and its respective dependent claims are not obvious in view of Raad et al. and Filho et al. Solely to expedite prosecution of the instant application, claims 1-3, 7-8, and 11 have been amended to recite a composition comprising an N-substituted maleimide and a cationic polypeptide.

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Applicant respectfully submits that the Examiner has not established a suggestion or motivation to combine Raad et al. and Filho et al. to produce the instant claims.

In the instant matter, the Examiner has not established a suggestion or motivation to combine Raad et al. with the N-phenylmaleimides disclosed in Filho et al. Raad et al. teaches an antimicrobial composition comprising a non-glycopeptide antimicrobial agent and a second agent selected from: (a) an anticoagulant, (b) an antithrombotic agent, and (c) a chelating agent. Raad et al. disclose that the non-glycopeptide antimicrobial agent includes non-glycopeptide antibiotics such as tetracyclines. No other examples of non-glycopeptide antimicrobial agents are provided. Further, Raad et al. define protamine sulfate as an anticoagulant and not for any antimicrobial properties. Filho et al. disclose bactericidal properties of certain N-phenylmaleimides. Filho et al. do not teach or suggest the usefulness of combining such compounds with another antimicrobial agent, nor in particular, with protamine sulfate. As such, the cited art does not teach or suggest the combination of N-substituted maleimides with cationic polypeptides to produce a composition to inhibit bacterial biofilms. Applicants respectfully assert that to combine N-substituted maleimides with the protamine sulfate based on the disclosure of Raad et al. (protamine sulfate as an anticoagulant) would have been hindsight reconstruction. *In re Oetiker*, 977 F.2d 1443, 1446 (Fed. Cir. 1992) ("There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination. That knowledge can not come from the applicant's invention itself.")

Additionally, Applicant demonstrates that combining a thiol specific reagent, and in particular, a N-substituted maleimide, with a cationic polypeptide yields the unexpected result of enhanced antibiofilm properties compared to the antibiofilm properties of either thiol specific reagents or cationic polypeptides alone. Examples 1, 2, 3, and 5 of the instant application clearly demonstrate the enhanced effects of combining a N-substituted maleimide (such as N'-(1,2-phenylene) dimaleimide (oPDM) or N-(1-pyrenyl) maleimide (PyrM) (thiol specific reagents) with a cationic polypeptide (protamine sulfate). For example, see page 26, paragraph [0110] and Figures 2, 3, and 6, which disclose enhanced inhibitory effects of oPDM + PS and PyrM + PS with respect to biofilm formation by *P. mirabilis*, *S. epidermis*, and *K. pneumoniae*. See also page 26, paragraph [0114] and Figures 8 and 12 that disclose an enhanced inhibitory effect of oPDM + PS and PyrM + PS with respect to biofilm formation.

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Neither Raad et al. nor Filho et al. teach or suggest the possibility of obtaining enhanced inhibition of bacterial biofilms by combining a N-substituted maleimide with a cationic polypeptide. Neither reference teaches the possibility of obtaining a composition that has enhanced inhibitory effects upon bacterial biofilms. Accordingly, it would not be obvious to combine a N-substituted maleimide with a cationic polypeptide to obtain a composition having enhanced antibiofilm properties exceeding the combined individual antibiofilm properties of a N-substitute maleimide and a cationic polypeptide.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a).

B. *Mebes et al. in view of Filho et al.* The Examiner rejects claims 1, 5-10, and 35 under 35 U.S.C. § 103(a) as being unpatentable over Mebes et al. (US Patent No. 4,845,256) in view of Filho et al. Applicant respectfully traverses.

Applicant maintains that the subject matter of original claim 1 and its respective dependent claims are not obvious in view of Mebes et al. and Filho et al. Solely to advance prosecution of the instant application, claims 9 and 35 have been cancelled, and claims 1, 7-8, and 10 have been amended. Claim 1, as amended, recites a composition for inhibiting bacterial biofilms on devices comprising a N-substituted maleimide and a cationic polypeptide. As amended, claim 1 does not recite a composition comprising a thiol specific agent and a quaternary ammonium compound. In view of the amended claims, Applicant respectfully asserts that the rejection is now moot.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a).

C. *Berry in view of Filho et al.* The Examiner rejects claims 1-2, 4-9, and 13-14 under 35 U.S.C. § 103(a) as being unpatentable over Berry U.S. Patent Application Publication No. 2002/0133169 in view of Filho et al. Applicant respectfully traverses.

Applicant maintains that the subject matter of original claim 1 and its respective dependent claims are not obvious claims in view of Berry and Filho et al. Solely to advance prosecution of the present application, claims 4, 9, and 13-14 have been cancelled, and claims 1-2 and 7-8 have been amended. As amended, claim 1 recites a composition for inhibiting bacterial biofilms on devices comprising a N-substituted maleimide and a cationic polypeptide. Claim 1 no longer recites a composition comprising an iron sequestering glycoprotein such as

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ovotransferin. In view of the amended claims, Applicant respectfully asserts that the rejection is now moot.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a).

D. Raad et al. in view of Filho et al. and further in view of Chinn et al. The Examiner rejects claims 1 and 15 under 35 U.S.C. § 103(a) as being unpatentable over Raad et al. in view of Filho et al. and further in view of Chinn et al. (U.S. Patent No. 6,528,107). Applicant respectfully traverses.

Applicant maintains that original claim 1 and its respective dependent claims are not obvious in view of Raad et al., Filho et al. and Chinn et al. Solely to advance prosecution of the present application, claim 1 has been amended to recite a composition for inhibiting bacterial biofilms on devices comprising a N-substituted maleimide and a cationic polypeptide.

As discussed above, Raad et al. and Filho et al. do not teach or suggest an enhanced composition for inhibiting bacterial biofilm formation. As discussed above, the instant application discloses enhanced properties of N-substituted maleimides and cationic polypeptides. The instant application demonstrates the enhanced inhibitory effects at page 26, paragraph [0110], Figures 2, 3, and 6, which disclose enhanced inhibitory effects of oPDM + PS and PyrM + PS with respect to biofilm and at page 26, paragraph [0114], and Figures 8 and 12, which disclose enhanced effects of oPDM + PS and PyrM + PS with respect to biofilm formation. As discussed above, there is no motivation or suggestion in either Raad et al. and Filho et al. to combine a N-substituted maleimide with a cationic polypeptide to obtain a composition having enhanced antibiofilm properties. Applicant further respectfully asserts that claims 1 and 15 are not obvious in view of Raad et al., Filho et al. and Chinn et al. since none of the cited art teaches or suggests the possibility of obtaining an enhanced inhibition of bacterial biofilms by combining a N-substituted maleimide with a cationic polypeptide.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a).

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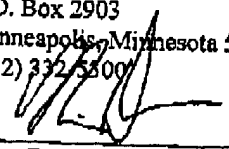
CONCLUSION

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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